REMARKS

Favorable reconsideration of the subject application as amended above is respectfully requested in view of the comments below.

Claims 1-34 are pending in the present application. Claims 1-17, 20-24 and 26-33 previously have been canceled. Claim 18 has been amended to delete the term "about." New claims 35 and 36 are added herein. Accordingly, claims 18, 19, 25 and 34-36 are presented for examination on the merits.

New claims 35 and 36 are added merely to break out subject that matter that has been searched and is allowable. No new matter is added by these amendments to the claims, nor is further searching required since a search of the subject matter of claim 18 and 25 necessitated a search specific to the subject matter of these claims.

Claim 34 has been amended to delete language that does not alter the scope of the claim and which is not essential to an understanding of what is being claimed. No new matter is added by this amendment, since the amendment is clerical in nature.

I. Rejection of Claims 18, 19, 25 and 34 stand Under 35 U.S.C. § 112, first paragraph

Claims 18, 19, 25 and 34 stand rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts that the specification contains insufficient information to support the genus encompassed by the claims because the species within the genus are highly variant.

This rejection is respectfully traversed as follows.

The specification provides written description of the claimed chimeric polypeptides, vaccines and their use. The specification teaches how to generate chimeric polypeptides and specifically discloses fragments of BVH3 and BVH-11 polypeptides that have at least about 85% sequence

identity with New 60 and New 56, the two components of the chimeric polypeptide of SEQ ID NO:332. For example, the specification provides description, and in particular sequence information of the following chimeric polypeptides: SEQ ID NOS: 336, 338, 348, 384, 334, 347 AND 376, which share at least about 85% sequence similarity to these two components of SEQ ID NO:332. As shown in the accompanying sequence alignments these polypeptides share the following sequence identity with SEQ ID NO: 332:, SEQ ID NO:336 - 98.7 %; SEQ ID NO: 338 - 98%; SEQ ID NO:348 – 97.9%; SEQ ID NO:384 - -85.1%; SEQ ID NO:334 – 99.3%; SEQ ID NO: 337 – 98.6%; and SEQ ID NO: 347 – 98.5%. These polypeptides are described in Tables H or G of the specification. As such, the specification provides sufficient written description support for the claimed invention.

Accordingly, the rejection of claims 18, 19, 25 and 34 under 35 U.S.C. § 112, first paragraph is respectfully traversed.

II. Rejection of Claims 18, 19, 25 and 34 Under 35 U.S.C. § 112, first paragraph (Enablement)

Claims 18, 19, 25 and 34 remain rejected under 35 U.S.C. §.112, first paragraph as allegedly not being enabled by the specification.

This rejection is respectfully traversed as follows.

The present application claims priority from and incorporates by reference co-pending US application 09/471,255 (the '255 application). Example 12 of the '255 application describes the cloning and expression of a chimeric gene encoding for a chimeric polypeptide corresponding to the carboxy-terminal region of BVH-3 in fusion at the C' end to the carboxy-terminal region of BVH-11 (NEW 12). This example also describes the additive protection observed after

vaccination of an animal with a chimeric polypeptide of present claim 1. NEW 12 is also described in the present application.

It is clear from the studies described in the present application that BVH-3 and BVH-11 are serologically distinct molecules simultaneously present on S. pneumoniae. The results of immunological studies of mice indicate that both proteins are good vaccine candidates. These proteins have the potential to provide protection against all pneumococci, regardless of serotype. Even though the two proteins share epitopes and sequences, they have different characteristics and may serve different biological functions. Thus, immunization against the two proteins may provide even higher levels of protection than that imparted by each individually. To examine this, several avenues where full-length or truncated BVH-3 and BVH-11 are administered in conjugation were explored.

Example 12 of the '255 application describes the genetic engineering of NEW12 and the use of NEW12 protein (NEW 1-KL-NEW 13, *i.e.*, BVH3' end (amino acids 472-1039; Figure 6 and SEQ ID NO:6)) - KL – BVH11 C' end (amino acids 354-840; (Figure 7 and SEQ ID NO:7), as an effective vaccine.

Briefly, BVH-3 and BVH-11 gene fragments corresponding to the 3'end of the genes were amplified by PCR using pairs of oligonucleotides engineered to amplify fragments spanning nucleotides 1414 to 3117(**SEQ ID NO: 1)** and nucleotides 1060 to 2520 (**SEQ ID NO: 3)** from S. pneumoniae strain SP64 BVH-3 and BVH-11 genes, respectively. The recombinant chimeric polypeptide, termed NEW 12, was expressed as a C-terminal fusion and purified.

Example 12 of the '255 application discloses that groups of eight female BALB/c mice (Charles River) were immunized subcutaneously two times at three-week intervals with 25 μg of either affinity purified His•Tag-fusion NEW1, BVH-11B or NEW12 protein in presence of 15 μg of QuilA adjuvant. Ten to 14 days following the last immunization, the mice were challenged with virulent S. pneumoniae. As demonstrated before, NEW1 and BVH-11B molecules comprising amino acids 472 to 1039 from BVH-3 protein and amino acids 354-840 from BVH-11 protein, respectively, correspond to portions of the proteins capable of eliciting a protective immune response. The chimeric NEW12 protein, elicited protection against the mouse-virulent strains WU2 and P4241. Seven out of 8 mice immunized with NEW12 were still alive ten days after the challenge while 28 out of 32 mice immunized with NEW1, BVH-11B, BVH-3M or adjuvant

alone were dead by five days post-challenge. Thus, vaccination of mice with NEW12 provided the highest degree of protection against WU2 challenge. These results indicate that immunization with a chimeric polypeptide of the invention provides additional protection to that obtained by administration of BVH-3 or BVH-11 antigens alone.

Evaluation of protection elicited by vaccination of mice with the chimeric NEW12 molecule is shown in the Table below(Table 9 of the '255 application).

	Challenge with WU2		Challenge with P4241	
Immunogen	Alive : dead[a]	Median day Alive	Alive : dead	Median day Alive
None	0 : 8	1	0 : 8	5
NEW1	2 : 6	2	1 : 7	8
BVH-11B	1 : 7	3.5	8 : 0	>14
NEW12	6 : 2	>14	7 : 1	>14
BVH-3M	1 : 7	3	8 : 1	>14

The specification also teaches that it is possible to construct other chimeric polypeptides, for example, as a result of a simultaneous expression of New 1 and New 4, New 1 and New 5, New 1 and New 10, or New 1 and New 14, and so on. The construction can be with New 1 upstream or downstream of New 4, New 5, New 10, BVH-11B or New 14. It is also possible to construct other chimeric polypeptides as a result of a simultaneous expression of more than two fragments of either genes of BVH-3, BVH-11 or BVH-11-2. The changes to the amino acid sequences can be made by using amino acid alignment tables, which are commonly used in the art, to make changes to those sites that are in an area most likely to have no negative effect on immunogenicity of the resulting polypeptide. These constructs can be made to have any degree of similarity to SEQ ID NO:332, including about 85%, and as discussed above, several chimeric polypeptides of the invention having at least about 85% sequence similarity to SEQ ID NO: 332 have been constructed using various polypeptide fragments of BVH-3 and BVH-11 that have been shown to confer an immunoprotective response.

Thus, the specification provides an enabling disclosure of the claimed invention.

Accordingly, the rejection of claims 18, 19, 25 and 34 under 35 USC § 112, first paragraph is respectfully traversed.

III. Rejection of Claims 18, 19 and 25 Under 35 USC § 112, second paragraph

It is respectfully submitted that the amendment to claim 18 renders this formal ground of rejection moot.

IV. rejection of Claim 34 Under 35 USC § 112, second paragraph

It is respectfully submitted that the rejection of claim 34 is rendered moot by the amendments above.

It is respectfully submitted that the present application, as amended above, is in condition for allowance, an early notification thereof being earnestly solicited. If any issues remain outstanding, the Examiner is respectfully requested to contact the undersigned attorney so that prosecution of this application may be expedited.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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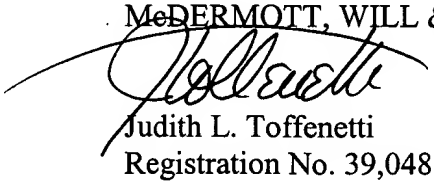

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